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5.30.004

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	February 18, 2011
Subject:	Carbaglu	**Page:**	1 of 4

Last Review Date: March 8, 2024

Carbaglu

Description

Carbaglu (carglumic acid)

Background
Carbaglu (carglumic acid) is used to treat certain conditions that result in hyperammonemia (excess ammonia) in the blood. Carbaglu treats hyperammonemia by acting as a replacement for N-acetylglutamate (NAG) in the urea cycle, whose role is the disposition of ammonia. NAG acts as the activator of carbamoyl phosphate synthetase 1 (CPS 1), a mitochondrial liver enzyme which catalyzes the first reaction of the urea cycle. The urea cycle includes a series of biochemical reactions in the liver resulting in the conversion of ammonia into urea, which is then excreted through the urine. Carbaglu acts as a CPS1 activator, improves or restores the function of the urea cycle, and facilitates ammonia detoxification and urea production (1).

Regulatory Status
FDA-approved indications: Carbaglu (carglumic acid) is a carbamoyl phosphate synthetase 1 (CPS 1) activator indicated in pediatric and adult patients as: (1)

- Adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency
- Maintenance therapy for the treatment of chronic hyperammonemia due to NAGS deficiency
- Adjunctive therapy to standard care for the treatment of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA)

Management of hyperammonemia due to NAGS deficiency, propionic acidemia or methylmalonic acidemia should be done in coordination with medical personnel experienced in

metabolic disorders. Ongoing monitoring of plasma ammonia levels, neurological status, laboratory tests and clinical responses in patients receiving Carbaglu is crucial to assess patient response to treatment (1).

The safety and effectiveness of Carbaglu for the treatment of pediatric patients aged birth to 17 years of age have been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Carbaglu may be considered **medically necessary** if the conditions indicated below are met.

Carbaglu may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. N-acetylglutamate synthase (NAGS) deficiency
2. Propionic acidemia (PA)
3. Methylmalonic acidemia (MMA)

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 2 years

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Carbaglu (carglumic acid) is used to treat certain conditions that result in hyperammonemia (excess ammonia) in the blood. Carbaglu treats hyperammonemia by acting as a replacement for N-acetylglutamate (NAG) in the urea cycle, whose role is the disposition of ammonia. NAG acts as the activator of carbamoyl phosphate synthetase 1 (CPS 1), a mitochondrial liver enzyme which catalyzes the first reaction of the urea cycle. The urea cycle includes a series of biochemical reactions in the liver resulting in the conversion of ammonia into urea, which is then excreted through the urine. Carbaglu acts as a CPS1 activator, improves or restores the function of the urea cycle, and facilitates ammonia detoxification and urea production (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Carbaglu while maintaining optimal therapeutic outcomes.

References

1. Carbaglu [package insert]. Lebanon, NJ: Recordati Rare Diseases, Inc.; August 2021.

Policy History

Date	Action
September 2012	Annual editorial review and reference update
June 2013	Annual editorial review and reference update
September 2014	Annual editorial review and reference update
September 2015	Annual review
September 2016	Annual editorial review and reference update Policy number change from 5.08.04 to 5.30.04
December 2017	Annual review and reference update
November 2018	Annual review and reference update
December 2019	Annual editorial review and annual review. Changed approval duration from lifetime to 2 years
December 2020	Annual review and reference update

February 2021	Addition of indications: propionic acidemia (PA) and methylmalonic acidemia (MMA)
March 2021	Annual review
March 2022	Annual review and reference update
December 2022	Annual review. Changed policy number to 5.30.004
March 2023	Annual review
March 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.